FOUNDATION OF THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

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11TH CONGRESS OF THE SOCIETY FOR THE STUDY OF NEUROPROTECTION AND NEUROPLASTICITY

1 - 3 OCTOBER, 2015

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SCIENTIFIC PROGRAM

OCTOBER 2ND, 2015

08:45 – 09:00 *WELCOME ADDRESS:*
Dafin F. Muresanu (Romania), Natan Bornstein (Israel)

PRESIDENTIAL SESSION, CHAIRPERSONS: Natan Bornstein (Israel), Dafin F. Muresanu (Romania)

09:00 – 09:30 Dafin F. Muresanu (Romania)
Shifting the paradigm in brain protection and recovery – the role of pharmacological support

09:30 – 10:00 Natan Bornstein (Israel)
Mood and gait as the interacting modulators of cognitive impairment after stroke

SESSION 1, CHAIRPERSONS: Anton Alvarez (Spain), Stephen Skaper (USA)

10:00 – 10:20 Hari Shanker Sharma (Sweden)
Pathophysiology of the blood-brain barrier in CNS injury & repair. New roles of trophic factors and nanomedicine including high altitude brain injury

10:20 – 10:40 Volker Hömberg (Germany)
The dilemma of cognitive rehabilitation

10:40 – 11:00 Fernando Góngora (Mexico)
Neurovascular reactivity, cognitive impairment and dementia

11:00 – 11:15 *DISCUSSIONS*

11:15 – 11:40 *COFFEE BREAK*

SESSION 2, CHAIRPERSONS: Antonio Federico (Italy), Peter Jenner (UK)

11:40 – 12:00	Marc Fisher (USA) Developing novel stroke therapies to enhance and complement current reperfusion therapy
12:00 – 12:20	Wolf-Dieter Heiss (Germany) From conventional concepts to a new paradigm in the treatment of ischemic stroke
12:20 – 12:40	Gregory del Zoppo (USA) Microvessel structural and permeability modulation in CNS injury, and the consequences for perfusion
12:40 – 13:00	Jaroslaw Aronowski (USA) Neuronal IL-4 in cytoprotection and recovery after ischemic stroke
13:00 – 13:15	*DISCUSSIONS*
13:15 – 14:10	*LUNCH*

SESSION 3, CHAIRPERSONS: Marc Fisher (USA), Gregory del Zoppo (USA)

14:10 – 14:30	Peter Jenner (UK) Novel pharmacological approaches to the treatment of Parkinson's disease
14:30 – 14:50	Ovidiu Bajenaru (Romania) Vitamin D and Parkinson's disease – possible pathogenetic pathways
14:50 – 15:10	Antonio Federico (Italy) Update on neurometabolic extrapyramidal genetic disorders: clinical and molecular-biochemical findings
15:10 – 15:30	Dieter Meier (Austria) Disease-modifying therapies in Parkinson's disease and other synucleinopathies
15:30 – 15:45	*DISCUSSIONS*

SESSION 4, CHAIRPERSONS: Ovidiu Bajenaru (Romania), Wolf-Dieter Heiss (Germany)

15:45 – 16:05	Roberto Maturana (Chile) The relevance of non-interventional studies in stroke assessment (CREGS-S Methodology case)
16:05 – 16:25	Roberto Ventura (Uruguay) Neuropsychiatric aspects for the treatment of closed TBI
16:25 – 16:45	Ignacio Previgliano (Argentina) The muscle as an endocrine organ and the muscle-brain's relationship
16:45 – 17:00	*DISCUSSIONS*
17:00 – 17:15	*COFFEE BREAK*

SESSION 5, CHAIRPERSONS: Volker Hömberg (Germany), Hari Shanker Sharma (Sweden)

17:15 – 17:35	Anton Alvarez (Spain) Neurorestoration in Alzheimer's disease: Synergistic effects of trophic factors
17:35 – 17:55	Jefferson V. Proaño (Mexico) The role of neurotrophic factors in Mild-to-Moderate Alzheimer's disease: A meta-analysis of randomized controlled clinical trials
17:55 – 18:15	Stephen Skaper (USA) Co-ultramicronized palmitoylethanolamide/luteolin promotes maturation of rat cortical oligodendrocytes and improves outcome in experimental autoimmune encephalomyelitis
18:15 – 18:30	*DISCUSSIONS*
18:30	*CLOSING REMARKS*


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ABSTRACTS

NEURORESTORATION IN ALZHEIMER'S DISEASE: SYNERGISTIC EFFECTS OF TROPHIC FACTORS

ANTON ALVAREZ[1]

O. IGLESIAS[1], M. ALEIXANDRE[2], C. LINARES[3], J. FIGUEROA[1,4], D. MURESANU[5], H. MOESSLER[6]

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Drugs approved for Alzheimer's disease (AD) treatment provide some symptomatic relief to the patients without evidence of disease modification, and clinical trials with therapeutic agents reducing amyloid and tau pathology, particularly vaccines showed no clinical efficacy up to now. Thus, strategies aimed at enhancing the endogenous processes of neurorestoration could represent an effective option for delaying AD onset and/or cognitive decline.

Neurotrophic factors such as nerve growth factor (NGF), brain derived neurotrophic factor (BDNF) and insulin-like growth factor-I (IGF-I) are downregulated in the brains of mild cognitive impairment and AD patients, suggesting that a deficit of brain trophic activity constitutes an early event in AD pathology. These neurotrophic factors are essential regulators of the mechanisms of neuroplasticity and brain repair required for neurorecovery and for the improvement of cognition. However, its therapeutic use has several important limitations such as their rapid enzymatic inactivation and low uptake through the blood-brain barrier (BBB). Trying to overcome these limitations, several naturally cleaved peptides, synthetic analogues and mimetic peptides are being investigated as alternatives for AD therapy.

In an attempt to test our hypothesis that neurotrophic compounds might support cholinotropic activities contributing to enhance and/or prolong the clinical effects of cholinesterase inhibitors (ChEIs) in AD, we compared the efficacy of the neurotrophic compound (10 ml; n=64), donepezil (10 mg; n=66) and a combination of both treatments (n=67) in mild-to-moderate (mini-mental state examination-MMSE score 12-25) probable AD patients enrolled in a 28-week, randomized, double-blind trial. Results indicate that improvements in global outcome (CIBIC+) favored the neurotrophic compound and the combination therapy, and that cognitive performance (ADAS-cog+) improved in all treatment groups with best scores in the combined therapy group at all study visits. In addition, the rate of combined responders (improvements in both cognition and global outcome) declined from week-16 to week-28 in patients on monotherapy and was maintained in patients receiving the combination therapy, which suggest a long-term synergistic effect of both drugs.

We recently reported reduced levels of serum BDNF levels in AD patients with apathy and in female AD patients carrying the APOE E4 allele. Apathy and dysphoria interacted to reduce circulating BDNF in patients without SSRIs treatment, and treatment with SSRIs was associated to a significant increase of BDNF levels in AD patients showing a positive response (no apathy or dysphoria). Our results indicated independent associations of apathy and APOE4 with reduced serum BDNF levels in AD, and are suggesting that BDNF reductions might contribute to the worse cognitive performance exhibited by apathetic patients and female APOE4 carriers. Since BDNF deficits influence AD pathology and low circulating BDNF may promote cognitive deterioration, we investigated the effects of neurotrophic factors, donepezil and the combined therapy on serum BDNF levels measured at baseline, week 16 and week 28 (endpoint) in the patients included in the aforementioned clinical trial.

The neurotrophic factors increased serum BDNF at week-16 (p=0.023), while the combination therapy enhanced it at both week-16 (p=0.007) and study endpoint (p=0.028). BDNF responses were signifi cantly higher in the combination therapy group than in donepezil (p=0.023) and Cerebrolysin (p=0.035) groups at week-16 and week-28, respectively. Changes in BDNF and IGF-1 at endpoint correlated positively in neurotrophic factors-treated groups (p=0.015). Overall, BDNF increases were greater in patients with apathy-depression and APOE4 than in the rest of patients at week-16 (p=0.028) and week-28 (p=0.020). In APOE4 patients treated with neurotrophic factors and the combined therapy, higher BDNF levels at baseline and week-16 were associated with better cognitive improvements at both week-16 and week-28 (p<0.01).

Our results indicate a synergistic action of neurotrophic factors to increase serum BDNF, suggest the involvement of BDNF in the cognitive eff ects of neurotrophic factors, and support a preventive role of BDNF for delaying cognitive decline in AD, at least in APOE4 carriers. BDNF changes reported here are in agreement with clinical observations showing that patients on the combined therapy maintained cognitive and global improvements till week-28, whereas those receiving monotherapy tended to lose part of their improvements after week-16. Finally, these fi ndings provide new insights on the relevance of neurotrophic factors in AD pathology and therapy.

NEURONAL IL-4 IN CYTOPROTECTION AND RECOVERY AFTER ISCHEMIC

JAROSLAW ARONOWSKI

University of Texas Health Science Center, Department of Neurology, Houston, Texas, USA

Following ischemic stroke, various damage-associated molecules are released from the ischemic core and diffuse to the ischemic penumbra, activating microglia and promoting pro-inflammatory responses that may cause damage to the local tissue. Here we demonstrate using *in vivo* and *in vitro* models that during sub-lethal ischemia, local neurons rapidly produce IL-4, a cytokine with potent anti-inflammatory properties. One such anti-inflammatory property includes its ability to polarize macrophages away from a pro-inflammatory M1 phenotype to a "healing" M2 phenotype. Using an IL-4 reporter mouse, we demonstrated that IL-4 expression was preferentially induced in neurons in the ischemic penumbra, but not in the ischemic core or in brain regions that were spared from ischemia. When added to cultured microglia, IL-4 was able to induce expression of genes typifying the M2 phenotype and PPARγ activation. IL-4 also enhanced expression of the IL-4 receptor on microglia, facilitating a "feed forward" increase in 1) their expression of trophic factors, and 2) PPARγ-dependent phagocytosis of apoptotic neurons. Parenteral administration of IL-4 resulted in augmented brain expression of M2- and PPARγ-related genes. Furthermore, IL-4 and PPARγ agonist administration improved functional recovery in a clinically-relevant mouse stroke model, even if administered 24 hours after the onset of ischemia.

We propose that IL-4 is secreted by ischemic neurons as an endogenous defense mechanism, playing a vital role in the regulation of brain cleanup and repair after stroke. Modulation of IL-4 and its associated pathways could represent a potential target for ischemic stroke treatment.

VITAMIN D AND PARKINSON'S DISEASE – POSSIBLE PATHOGENETIC PATHWAYS

OVIDIU-ALEXANDRU BAJENARU
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University of Medicine and Pharmacy "Carol Davila" Bucharest, Romania

More and more data suggest a link between a low seric level of vitamin D and the development of Parkinson's disease and other diseases of the central nervous system like mutiple sclerosis and Alzheimer's disease. While the relationship between vitamin D and bone density is well known since more than a century, the pathways linking vitamin D to these CNS diseases are nowadays a matter of debate and research. The data in the recent published studies, suggest the nuclear vitamin D receptors which have a particular distribution in the CNS structures involved in PD pathogenetic pathways could mediate this link, influencing the expression of some particular genes in these patients. If this mechanisms could facilitate the phenotypic expression in persons with genetic predisposition to PD seem to be an attractive hypothesis but yet still unproven; if other metabolic and immune effects of vitamin D deficiency could influence this relationship is still unknown. These potential relationships of vitamin D with other pathogenetic pathways and risk factors involved in PD pathogenetic mechanisms will be presented, as they potentially could be the basis for new research.

MOOD AND GAIT AS THE INTERACTING MODULATORS OF COGNITIVE IMPAIRMENT AFTER STROKE

NATAN BORNSTEIN
Tel-Aviv Sourasky Medical Center, Sackler School of Medicine, Tel-Aviv University, Israel

Background: After a stroke, patients frequently experience a spectrum of neuropsychological and motor deficits, resulting in impaired activities, cognitive and function.
Additionally, post-stroke (PS) depression is associated with increased mortality, disability and anxiety levels, and lower quality of life.
We tested whether the assessment of balance and gait, as well as depressive symptoms, can enhance the prediction of long-term cognitive and functional outcome in stroke survivors.

Methods: Participants were first-ever, mild-moderate stroke/ patients from the TABASCO study, who underwent 3T MRI and followed using neurologic, neuropsychological, mobility and functional examinations 6, 12 and 24 months after the index event.

Results: Data were available for 306 consecutive patients. Of these patients, 51 (16.7%) developed cognitive decline (CD) within 2 years.
Multivariate regression analysis showed that a Geriatric Depression Score (GDS) > 6 at admission and 6 months PS was a significant independent marker of CD and worse functional outcome 2 years after the index event (OR=3.68, 95% CI: 1.03-13.21).
The CD group and cognitively intact (CI) group did not differ in their neurological deficits nor in their infarct volume or location. Nonetheless, 6 months PS, the Timed Up and Go (TUG) test took longer in those who later developed CD ($p<0.001$) and they had lower Berg Balance Scale scores ($p<0.001$) and slower gait ($p<0.001$). Another multivariate regression model showed that TUG longer than 12 seconds at 6 months PS was a significant independent risk marker of CD 2 years PS (OR=6.07, 95% CI: 1.36-27.15).

Conclusions: We suggest that measures of balance and gait as well as depression scores are significant risk markers of cognitive status 2 years after stroke. Relatively simple, performance-based tests of mobility and depression screening may enhance the identification of stroke/TIA survivors who have an increased risk to develop cognitive decline and may benefit from closer medical surveillance.

UPDATE ON NEUROMETABOLIC EXTRAPYRAMIDAL GENETIC DISORDERS: CLINICAL AND MOLECULAR-BIOCHEMICAL FINDINGS

ANTONIO FEDERICO

Department of Medicine, Surgery and Neurosciences, Medical School, University of Siena, Siena, Italy

Extrapyramidal disorders are mainly linked with Parkinson's neurodegeneration of dopaminergic pathway. These conditions may be also secondary to several neurometabolic disorders impairing dopaminergic pathway. We will report Disorders of Heavy Metal Metabolism , Disorders of Neurotransmitter Metabolism , Disorders of energy metabolism, Lysosomal Diseases , Disorders of intermediary metabolism , Disorders of mechanism of DNA Damage and Repair , all mainly presenting with prevalent extrapyramidal features.
We here will report our experience in the diagnosis and treatment of these conditions, describing the clinical, the biochemical and the therapeutic aspects.
We will discuss a recently described by our group genetic form of parkinsonism associated with a defect in the transport of manganese and in which chelating therapy by EDTA results in a marked improvement of all symptoms and finally we will report our experience in the clinical and molecular investigations in Basal ganglia calcifications syndromes (Fahr syndrome and similar conditions).

DEVELOPING NOVEL STROKE THERAPIES TO ENHANCE AND COMPLEMENT CURRENT REPERFUSION THERAPY

MARC FISHER

Department of Neurology, Beth Israel Deaconess Medical Center, Boston, MA, USA

The recently positive endovascular acute stroke trials provided convincing evidence that endovascular therapy in appropriately selected patients who are treated rapidly with a stent retriever substantially improves outcome. Many questions about who benefits remain and will require additional clinical trials. Additionally, adjunctive therapies can be envisioned to extend and enhance the beneficial effects on endovascular therapy. One novel approach would be to use neuroprotection initiated prehospital to extend the survival of the ischemic penumbra so that more patients have a small or moderate ischemic core when they are being considered for endovascular therapy. This approach would be particularly valuable in regions where endovascular centers are sparse and transport times are long. Another novel therapeutic approach will be to treat reperfusion injury now that many patients will have successful opening of their occluded intracranial vessel. Many potential approaches to impeding reperfusion injury can be considered but the clinical trials will be large and difficult to perform. Intravenous thrombolysis will remain the mainstay of acute stroke therapy around the world. In the endovascular trial control arms, it was observed that the reperfusion efficacy of tPA to a TICI 2B/3 range was modest, approximately 30-40%. Therefore, it is appropriate to consider developing i.v. thrombolytic approaches that can substantially increase this rate. Other thrombolytic drugs such as tenecteplase have this capability in animal models and are being evaluated in clinical trials. Another approach would be to enhance the thrombolytic efficacy of tPA by combining it with another molecule such as annexin-2. Animal studies with this combination have yielded interesting results supporting better thrombolytic efficacy and better safety than with tPA alone.

NEUROVASCULAR REACTIVITY, COGNITIVE IMPAIRMENT AND DEMENTIA

FERNANDO GÓNGORA

Neurology, Hospital Universitario, UANL, Monterrey, Mexico

Ischemic brain injury by small vessel disease represents the 25% of stroke cases. The reasons associated with occlusion of small arteries are blood vessel disease (lipohyalinosis), intracranial atherosclerosis vessel and embolic stroke in a proximal artery or heart[1].

In brain imaging studies such as magnetic resonance imaging, the presence of Leukoaraiosis, lacunar infarcts, microbleeds and dilation of the perivascular spaces suggest intrinsic arterial disease.

The brain endothelium regulates cerebral blood flow and integrity of the blood-brain barrier. Endothelial dysfunction of small arterial vessels (arterioles) can cause lacunar infarcts by failing to maintain self-regulation and neurovascular damage[2].

Patients with lacunar infarcts suffer disorders of cerebral blood reactivity when they are evaluated with cerebral blood flow studies[3].

Some series markers, such as von Willebrand factor, homocysteine and C-reactive protein highly sensitive, have been related with cerebral reactivity disorders[4].

In memory disorders, particularly Alzheimer's disease, it is remarked the higher risk of stroke, which rises the damage and accelerate functional impairment[5]. Similarly, in the early stages of the disease, some alterations were found in the mechanisms of brain vasomotor self-regulation[6].

The neurovascular theory of cognitive impairment complements our current understanding of the pathophysiology of dementia disorders, and new treatment options for microvascular protection are complementary to the current handling of dementia.

1. Cerebrovascular Dis. 2013;36:131-138.
2. Nature Medicine. 2005;11:923-924.
3. Int J Stroke. 2013;8(6):413-421.
4. Cerebrovasc Dis. 2013;36:131-138.
5. Current Alzheimer Research. 2014;11:11-17.
6. Alzheimer and dementia. 2014;10(4):S804.

FROM CONVENTIONAL CONCEPTS TO A NEW PARADIGM IN THE TREATMENT OF ISCHEMIC STROKE

WOLF-DIETER HEISS

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The cause of ischemic stroke is a significant impairment of blood supply to the brain tissue. If the normal cerebral blood flow (CBF, mean 50 ml/100g.min, gray matter 60-80 ml/100g.min, white matter 20 ml/100g.min) is reduced below a certain level reversible functional failure occurs (functional threshold); a further decrease of CBF below a lower level leads to irreversible morphological damage (threshold for morphological intergrity). The tissue with perfusion values in the range between these limits is called the "ischemic penunmbra", which is characterized by the potential for functional recovery without morphological damage, provided that local blood flow can be reestablished within a certain time window, which is dependent on the residual flow. The translation of this experimental concept as the basis for efficient treatment of stroke requires non-invasive methods by which regional flow and energy metabolism can be repeatedly investigated. Positron emission tomography (PET) allows the quantification of cerebral blood flow, metabolic rate for oxygen and oxygen extraction fraction. By these variables a clear definition of irreversible tissue damage and of critically perfused but potentially

salvageable tissue (i.e. the penumbra) can be achieved. Further tracers can be used for early detection of irreversible tissue damage (central benzodiazepine receptor ligand flumazenil). As a widely applicable clinical tool perfusion / diffusion weighted magnetic resonance imaging is used, and the "mismatch" between the PW- and the DW-abnormalities might serve as an indicator of the penumbra, but has limitations. A multitude of electrical and biological disturbances interact in the progression of irreversible cell damage in ischemia. The events in the molecular cascade of injuries are interconnected in a complex way, which makes it difficult to predict their relative pathogenetic importance

Based on the concept of the penumbra improvement of perfusion within the time window of opportunity is still the primary goal in treatment of ischemic stroke, Neuroprotective and other strategies can only play a supportive role. Thrombolysis resulting from the intravenous administration of recombinant tissue plasminogen activator (rt-PA) within 4.5 h significantly reduces the incidence of death or dependency at 3 to 6 months, but the benefit of its administration ceases between 4.5 and 6 h after the ictus. Attempts to recanalize occluded vessels after this time window by intra-arterial rt-PA or mechanical thrombectomy enhance reperfusion and have recently been shown to improve clinical outcome in carefully selected patients. However, the number of patients who may benefit from these reperfusion therapies is small and probably totals less than 20% of all stroke victims, even for those treated at specialized centers

Neuroprotective and other directed at correcting one biochemical or molecular step in the pathophysiological cascade of ischemic cell damage have not shown efficacy in clinical trials. This failure might be due to the design of human trials, which often do not consider the limited time windows of targeted steps in the pathophysiological cascade or the complexity of the biochemical and molecular mechanisms leading to ischemic brain damage. The new paradigm of treatment of ischemic stroke therefore should include testing of a multi-targeted strategy that includes compounds with effects on several of the associated pathophysiologic events. The neurotrophic factors have been shown to have neuroprotective properties and to be effective against excitotoxicity and additionally, it has been demonstrated to exhibit neurotrophic activity, promote neuronal sprouting, improve cellular survival and stimulate neurogenesis. The treatments in these previous clinical trials were initiated during the acute phase after stroke and were mainly limited to 10 days. The neuroprotective effects have been primarily assessed, and its neurotrophic and neuroplastic effects on recovery have been neglected. Treatment of ischemic stroke therefore must be extended into the recovery phase.

THE DILEMMA OF COGNITIVE REHABILITATION

VOLKER HÖMBERG

Deptartment of Neurology, Heinrich Heine University, Düsseldorf, Germany

Beside sensory -motor-aspects of impairment and disability cognitive problems are the second most important target for neurorehabilita-tionin in all major ares of neurorehab (esp stroke and TBI) These encompass neuropsychological domains as attention, perception, memory and executive functions.

General rules of learning which are now commonly applied in the field of motor and sensory rehabilitation are more difficult to apply in the cognitive field. Furthermore beyond learning approaches directed primarily to facilitate compensation strategies, attempts to tackle impairments more directly are underdeveloped and have only occasionally been addressed.

In the talk the state of evidence base concepts in cognitive rehabilita-tion will be reviewed and perspectives of use of computer technology and virtual reality as well as ideas how to approach impairments will be discussed.

The differences between sensory-motor and cognitive rehabilitation will be discussed. Finally perspectives for future research needs will be presented.

NOVEL PHARMACOLOGICAL APPROACHES TO THE TREATMENT OF PARKINSON'S DISEASE

PETER JENNER

NDRC, Institute of Pharmaceutical Sciences, Faculty of Life Sciences and Medicine, King's College, London, UK

The drug treatment of Parkinson's disease (PD) has been based around dopamine replacement therapy for many decades. This improves motor function in early PD but many problems remain that relate the long term complications of dopaminergic therapy, the progression of the disease process and the occurrence of non-motor symptoms of PD. In essence the changes that are occurring in drug therapy can be divided in those that affect the early stages of PD, those which are to be employed in the later more complicated stages of the illness and those which might be disease modifying.

In early treatment, there has been a return to the use of L-dopa based on the results of PD-MED and STRIDE-PD trials which shows that careful early use has the best clinical efficacy and no long term disadvantage with respect to the appearance and severity of motor complications and motor fluctuations in later disease. As a consequence novel delivery forms of L-dopa are being developed along with new formulations for oral administration.

Dopamine agonists are the other main line therapy used in early and late PD but the only dopamine agonist drug that exhibits clinical efficacy equivalent to that of L-dopa is apomorphine. The acute subcutaneous injection of apomorphine is highly effective as a rescue therapy for unpredictable 'off' periods in patients taking oral dopaminergic drugs and experiencing 'wearing off'. The subcutaneous infusion of apomorphine can replace or supplement oral dopaminergic therapy when insufficient 'on' time is obtained and where alterations in oral medication produce no further benefit or intolerable side-effects appear. The infusion of apomorphine can also lead to a reduction in the intensity and duration of established dyskinesia on prolonged use. Apomorphine is administered subcutaneously as a result of its poor oral bioavailability. As a consequence, there is particular interest in developing new forms of apomorphine that will allow less invasive use and that will benefit from its proven clinical efficacy. Perhaps importantly, orally effective prodrug derivatives of apomorphine are under investigation. Why apomorphine is the best dopamine agonist probably relates to its ability to interact with both D-1 and D-2 dopamine receptors and its generally rich pharmacology which needs to be explored further.

Non-dopaminergic approaches to treating PD are under study as a means of improving the treatment of motor symptoms and suppressing dyskinesia but more importantly as a way forward for treating the non-motor components of the illness. The treatment of non-motor symptoms of PD has become a priority with an 'as needs' symptomatic approach being used currently as the neuronal basis of many non-motor symptoms is not clear. However, preclinical studies on cognition, sleep and autonomic change are starting to develop animal models in which novel pharmacological approaches can be tested. As an example of events happening around non-dopaminergic treatments, interesting new formulations of the weak NMDA receptor antagonist, amantadine are being studied for suppressing dyskinesia and other classes of glutamate antagonists are under investigation. However, it is the potential use of non-dopaminergic approaches to the treatment of 'wearing off' and dyskinesia where most effort has gone but so far with little clinical translation. One exception is the introduction of the adenosine A2a antagonist Istradefylline in to the treatment of PD for the control of 'wearing off'.

Lastly, the search for disease modifying/neuroprotective treatments continues despite previous failures. Attacking the accumulation of -synuclein is one such approach as is the search for drugs that modify other

components of the cell death cycle that are affected by gene defects detected in inherited forms of PD, such as parkin, LRRK2 and GBA. The use of antibody approaches to clear α-synuclein has gained momentum based on the recently reported success of similar strategies for amyloid dispersal in Alzheimer's disease. However, very early detection of pathology occurring in PD will be required if intervention is to occur at a point likely to arrest or slow disease progression. One other interesting approach is the repositioning of drugs already used in man for other indications but which have shown evidence for neuroprotection in preclinical studies. These include drugs used to treat type II diabetes and calcium channel blockers used in cardio-vascular disease.

THE RELEVANCE OF NON-INTERVENTIONAL STUDIES IN STROKE ASSESSMENT (CREGS-S METHODOLOGY CASE)

ROBERTO MATURANA

Head of the Stroke Unit and Neurology Unit, Neurology-Neurosurgery Department, Hospital DIPRECA, Santiago de Chile, Chile

Randomised clinical trials are the gold standard to de termine effi c a cy but are not practical in every circumstance. Registries can be invaluable for assessing eff e ctiveness and for studying routinely used treatments. Registration of patients can easily be done using Internet-based systems. Contrasts between patient groups are potentially subject to bias. However, many of the major sources of bias can be handled through application of a rigorous approach to selection, matching and independent, blinded assessments of outcome. Methods include the use propensity scores and propensity score matching, which account for covariates that predict receiving a treatment. A crucial aspect is pre-specifi cation of a detailed analysis protocol with separation of the matching and outcome assessment processes so that thematching process is completed before access to outcome assessments. Examples where these approaches are being used include the ongoing SITS OPEN study for thrombectomy in acute stroke and the CREGS cohort studies of neurotrophic factors in stroke recovery.

DISEASE-MODIFYING THERAPIES IN PARKINSON'S DISEASE AND OTHER SYNUCLEINOPATHIES

DIETER MEIER

Neuropore Therapies, Inc., San Diego, USA

Parkinson's Disease (PD) is a progressive neurodegenerative disease. The clinical manifestation can include motor and non-motor symptoms (eg. tremor, rigor, bradykinesia, postural instability and sleep disturbances, autonomic dysregulation impairment of cognition, alteration of affect). The neuropathological hallmark of PD and other synucleinopathies is the accumulation of alpha-synuclein (ASYN) containing cytosolic inclusions, called Lewy-bodies

Once correctly diagnosed, the symptomatic treatment of early Parkinson's Disease (PD) mainly based on dopaminergic therapies appears to be relatively straightforward . However, with progressing disease, and also possibly as a result of previous therapies, symptoms of later stages of PD become increasingly difficult to treat.

Several therapies have been proposed to not only alleviate the symptoms of PD but (also) to slow or halt the course of the disease progression. but to date, such putative 'Disease Modifying' approaches have not been borne out in rigourous clinical trials. This may be in part because: symptomatic effects have confounded the disease-modifying actions ; sensitive, validated biomarkers to measure disease progression are lacking and; the

term disease-modifying has been mis-applied to symptomatic treatments for promotional purposes.
To develop a truely disease-modifying therapeutic, it will be necessary to stop the progression of the underlying pathophysiology. A tremendous amount of research has been devoted to understanding the role of misfolding and aggregation of the synaptic protein alpha synuclein (ASYN). Both human genetic studies and experiments in animals provide compelling links between the dysregulation of ASYN and PD. As with other misfolded proteins, it is likely that in PD the microscopically detectable Lewy bodies containg ASYN polymers are final deposits while earlier stages of aggregates are involved in the pathogenic process. Recent studies further suggest that membrane-embedded oligomers of ASYN may be a particularly toxic form of ASYN, resulting in disruption of synaptic function, loss of cell membrane integrity and ultimately, in neuronal degeneration.
Treatments that prevent the formation and accumulation of these toxic membrane-embedded oligomeric aggregates of ASYN may prevent further decay or even restore synaptic function in impaired systems and slow the rate of degeneration, thus providing a therapeutic benefit for patients. Treatment approaches that target the misfolding and aggregation process are currently being explored in early clinical studies with both antibodies and small molecules.
Another, therapeutic principle is to enhance the clearance of these protein aggregates by rectifying defects in a dysregulated clearance mechanism . Approaches aimed at enhancing clearance are still at the animal-testing stage but hold out promise because they may prove to be effective even after the disease has progressed to its later stages.

In summary, while the physiological role of ASYN is currently not fully understood, it is clear that the accumulation of misfolded forms of ASYN contributes to the pathology of PD and that preventing the formation of toxic oligomers and enhancing cellular clearance mechanisms may be viable therapeutic approaches to halt or slow disease progression.

SHIFTING THE PARADIGM IN BRAIN PROTECTION AND RECOVERY – THE ROLE OF PHARMACOLOGICAL SUPPORT

DAFIN F. MURESANU
Chairman Department of Clinical Neurosciences, University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca, Romania

Brain damage affects all three levels of structural and functional organization: cellular and molecular level, circuitries level and dynamic network level and launches an endogenous continuous brain defense response which consists in neuroprotection (the immediate response) and neurorecovery (a later response).

Endogenous neuromodulation represents at the cellular and molecular level the optimization of common biological processes that could potentially generate cell death or promote neurodegeneration. At the circuitries and dynamic network levels, it represents the tendency in reinbalancing of functional connectivity in resting-state netwoks.

In the last years, there has been a substantial effort in understanding the brain functioning and how to enhance endogenous neuromodulation and neurorehabilitation in general, by using a large spectrum of neurotechnologies such as imaging techniques (functional magnetic resonance imaging, ligant-based positron emission tomography, diffusion-tensor imaging), quantitative electroencephalogram, magnetoencephalography, eye tracking, optogenetics, transcranial magnetic stimulation, transcranial direct current simulation, deep brain simulation, computational neuroscience and brain-computer interfaces. The combination between these technologies provide valuable information about the structure-function relationship underling resting-state networks, about the dynamic cross-talk between networks and about the abnormalities in the functional connectivity in different pathologies.

Neurorecovery can be enhanced by pharmacological intervention, physical activity, electromagnetic stimulation, psychological support, environmental stimulation or any demonstrated combinations of these factors capable of improving the patient's condition after brain and spinal cord injuries. From the pharmacological perspective, it is clear that the focusing on molecules that are capable of mimic the function of endogenous molecules with multimodal and pleiotropic neuroprotective effects is the best approach in neurorecovery, especially when they are associated with intensive physical training.

Biological agents (e.g., neurotrophic factors and related molecules) with modulating and multimodal effects are better pharmacological agents for brain and spinal cord protection and recovery, because they usually have also pleiotropic neuroprotective effect. That is why they are capable of pharmacologically bridging acute neuroprotective processes with the long-term recovery processes.

There are many animal and human studies trying to elucidate the cellular and molecular mechanisms of plasticity of the nervous system. A better understanding of the mechanisms underlying the neuroplasticity will reflect in a more efficient and comprehensive treatment.

This presentation will focus on the therapeutical effects of multimodal drugs on neurorecovery after brain lesion.

THE MUSCLE AS AN ENDOCRINE ORGAN AND THE MUSCLE-BRAIN'S RELATIONSHIP

IGNACIO PREVIGLIANO

Head Division of Intensive Care – Hospital Fernandez – Argentina
Prof. of Neurology – Neurology Chair – Universidad Maimonides – Argentina

Since Pedersen description of Interleukine 6 release according to exercise's intensity it was clear that the muscle could act as an endocrine organ releasing substances, called myokines nowdays, that should have endocrine, paracrine and autocrine actions. The muscle secretome consists of several hundred secreted peptides. This finding provides a conceptual basis and a whole new paradigm for understanding how muscles communicate with other organs such as adipose tissue, liver, pancreas, bones, and brain. In addition, several myokines exert their effects within the muscle itself.

Physical inactivity promotes an unbalance between these substances towards a pro-inflammatory status, thus favoring the vicious circle of sarcopenia, accumulation of fat - especially visceral - and development of cardiovascular diseases, type 2 diabetes mellitus, cancer, dementia and depression, according to what has been called "the diseasome of physical inactivity".

Brain derived neurotrophic factor (BDNF) is a member of the neurotrophic factor family, which plays a key role in regulating survival, growth, and maintenance of neurons, and also plays a role in learning and memory. But the main source for BDNF release is vigorous muscle contraction although muscle-derived BDNF appears not to be released into the circulation. So we can identified BDNF as a novel contraction-induced muscle cell-derived protein that exerts its effect either via autocrine or paracrine effects.

The purpose of this presentation will be to analyze the relationship between myokines and the central nervous system focus on disease generation, modification or healing.

THE ROLE OF NEUROTROPHIC FACTORS IN MILD-TO-MODERATE ALZHEIMER'S DISEASE: A META-ANALYSIS OF RANDOMIZED CONTROLLED CLINICAL TRIALS

JEFFERSON V. PROAÑO

Neurologist and Researcher, Medical Research Unit of Neurological Diseases, Hospital de Especialidades del Centro Médico Nacional Siglo XXI, Mexico

Objective: It was to provide a systematic and quantitative summary of benefit and risk of neurotrophic factors in patients with mild-to-moderate Alzheimer's disease (AD)

Design: This is a meta-analysis of randomized double-blind placebo-controlled clinical trials.

Data Sources: Trials were identified with the help of PubMed, the Cochrane Dementia Group database, the Center for Collaborative Neurosciences, and references from reviews; no language restrictions were applied.

Study Selection: All randomized double-blind placebo-controlled studies on 30 ml/day of Cerebrolysin in mild-to-moderate AD were included.

Results: There were 6 eligible randomized controlled trials comparing neurotrophic factors with placebo. For all studies, either individual patient data and/or published data (aggregate data) were available. Analyses were based on the odds ratio (OR) for dichotomized global clinical change and for safety criteria, on the standardized mean diff erence (SMD) for pooling of cognitive function, and on the Mann-Whitney statistic (MW) for multivariate analysis of 'global benefi t' (combined effect of global clinical change and cognitive function). The neurotrophic factors were was significantly more effective than placebo at 4 weeks regarding cognitive function, 4 weeks and 6 months regarding global clinical change and at 4 weeks and 6 months regarding 'global benefit

Conclusion: This meta-analysis provides evidence that neurotrophic factors have neurotrophic factors have an overall beneficial effect and a favorable benefit- risk ratio in patients with mild-to-moderate

AD. neurotrophic factor as a therapeutic agent should be considered by clinicians seeking treatment options for mild-to-moderate AD.

PATHOPHYSIOLOGY OF THE BLOOD-BRAIN BARRIER IN CNS INJURY & REPAIR. NEW ROLES OF TROPHIC FACTORS AND NANOMEDICINE INCLUDING HIGH ALTITUDE BRAIN INJURY

HARI SHANKER SHARMA[1]

DAFIN F. MURESANU[2], JOSÉ VICENTE LAFUENTE[3], Z RYAN TIAN[4], ASYA OZKIZILCIK[4], RANJANA PATNAIK[5], ARUNA SHARMA[1]

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4. Department of Chemistry & Biochemistry, University of Arkansas Fayetteville, AR, USA
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Recent advancement in nanomedicine suggests that nano drug delivery using nanoformulation enhances neurotherapeutic values of drugs or neurodiagnostic tools for superior effects than the conventional drugs or the parent compounds [1,2]. This indicates a bright future for nanomedicine in treating neurological diseases in clinics. However, effects of nanoparticles per se in inducing neurotoxicology, if any is still being largely ignored [3]. The main aim of nanomedicine is to enhance the drug availability within the central nervous system (CNS) for greater therapeutic successes. However, once the drug together with nanoparticles enters into the CNS compartments, the fate of nanomaterial within the brain microenvironment is largely remained unknown. Thus, to achieve greater success in nanomedicine our knowledge in expanding our understanding of nanoneurotoxicology in details is the need of the hour.

In addition, neurological diseases are often associated with several co-morbidity factors, e.g., stress, trauma, hypertension or diabetes. Recent observations show that brain injury occurring at high altitude (HA) could have adverse effects on the pathophysiological outcome. Thus, new research is needed to reduce HA induced exacerbation of brain pathology following trauma. These co-morbidity factors tremendously influence the neurotherapeutic potentials of conventional drugs. Thus, this is utmost necessary to develop nanomedicine keeping these factors in mind. Recent research in our laboratory demonstrated that engineered nanoparticles from metals used for nanodrug delivery significantly affected the CNS functions in healthy animals. These adverse reactions of nanoparticles are further potentiated in animals associated with heat stress, diabetes, trauma or hypertension at HA. These effects nanomaterials were dependent on their composition and the doses used. Thus, drugs delivered using TiO2 nanowired enhanced the neurotherapeutic potential of the parent compounds following CNS injuries in healthy animals. However, almost double doses of nanodrug delivery are needed to achieve comparable neuroprotection in animals associated with anyone of the above co-morbidity factors. Thus, the neurotrophic factor delivered either though TiO2-nased nanowires or PLGA-nanoparticles effectively reduced brain pathology in several diverse neurological diseases often complicated with various co-morbidity factors. Our observations showed that TiO2 neurotrophic factors are is also effective in brain injury performed at HA conditions in both cold & hot environment. These observations are the first to show that it could be useful in HA pathology in military personnel, pilots and injured soldiers airlifted for treatment. Taken together, it appears that while exploring new nanodrug formulations for neurotherapeutic purposes, co-morbidly factors and composition of nanoparticles require great attention. Furthermore, neurotoxicity caused by nanoparticles per se should be examined in greater details at normal altitude vs. HA before using them for nanodrug delivery in patients.

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CO-ULTRAMICRONIZED PALMITOYLETHANOLAMIDE/ LUTEOLIN PROMOTES MATURATION OF RAT CORTICAL OLIGODENDROCYTES AND IMPROVES OUTCOME IN EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS

STEPHEN D. SKAPER
MASSIMO BARBIERATO, GABRIELLA CONTARINI, CARLA MARINELLI, LAURA FACCI, PIETRO GIUSTI
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Oligodendrocytes are the myelin-producing cells of the central nervous system responsible for ensheathment of axons. Oligodendrocytes have limited ability to repair the damage to themselves or to other nerve cells, as seen in multiple sclerosis (MS), a chronic neuroinflammatory demyelinating disorder of the central nervous system with a strong neurodegenerative component. MS lesions are characterized by the presence of undifferentiated oligodendrocyte precursor cells (OPCs), highlighting their inability to mature into myelin-producing oligodendrocytes. Thus, an important strategy may be to replace the lost oligodendrocytes and/or promote their maturation or proliferation. N-palmitoylethanolamine (PEA) is an endogenous fatty acid amide belonging to the N-acylethanolamines family. Studies demonstrate PEA to possess analgesic, anti-inflammatory, and neuroprotective actions. More recently, a composite of co-ultramicronized PEA and the flavonoid luteolin (co-ultramicronized PEA/Lut, 10:1 by mass) was shown to be more efficacious that PEA alone in improving outcome in experimental models of spinal cord injury and traumatic brain injury. Here, we examined the ability of co-ultramicronized PEA/Lut to promote progression of OPCs into a differentiated phenotype. OPCs were prepared from newborn rat cortical mixed glial cell cultures as described, and treated the following day with 10 μM co-ultramicronized PEA/Lut. Cells were collected 1, 4 and 8 days later and analyzed for expression of myelin basic protein (MBP). Real-Time Polymerase Chain Reaction and Western blot analyses revealed a time-dependent increase in expression of both mRNA for MBP and MBP content by immunoblotting. Treatment with either ultramicronized PEA or luteolin was ineffective. Moreover, co-ultramicronized PEA/Lut improved clinical score in myelin oligodendrocyte glycoprotein (MOG35-55) induced experimental autoimmune encephalomyelitis

in C57BL/6 mice, often used as a chronic monophasic model of MS. Co-ultramicronized PEA/Lut may represent a novel pharmacological strategy to promote OPC maturation and remyelination in MS.

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NEUROPSYCHIATRIC ASPECTS FOR THE TREATMENT OF CLOSED TBI

ROBERTO VENTURA

Neuropsychology Assistant Professor at Neurology Institute, Associate professor of Biological Bases of Human Behavior at Psychology University, Uruguay

The brain is the part of the central nervous system contained in the cranial cavity. The brain is the organ that allows us to organize our psyche and pre-frontal activities, organizing our relationships with the environment. Consisting of cognitive behavioral networks both intra- and inter-hemispheric, the brain can be affected by different pathologies, both in the development and in the adulthood (like degenerative, trauma, infection, tumors, etc.), which lead to various diseases that are analyzed by psychiatrist and neurologists. Closed Head Injury (CHI) is one of the most common causes of brain injury and of the diffuse axonal injury which is the most common cause of the attention and memory disorders, dysexecutives syndromes and changes of the personality.

The cognitive impairment related disorders like changes of mood, psychosis and schizophrenia, emphasize the importance of the mechanism of the frontal lobe. This presentation is divided in two different parts. The first one is about the "neuropsychiatric disorders as consequences of a closed head injury" with socio-familiar repercussions. The second one is focused on the "pre-frontal syndromes" in order to better understand the world of post-traumatic brain injury. Both presentations are based on the semiotic clinical approach to CHI, but also on its diagnostic and therapeutic implications.

MICROVESSEL STRUCTURAL AND PERMEABILITY MODULATION IN CNS INJURY, AND THE CONSEQUENCES FOR PERFUSION

GREGORY DEL ZOPPO

Department of Medicine, Department of Neurology, University of Washington School of Medicine Seattle, Washington, USA

Acute processes in the evolution of cerebral vascular injury caused by focal ischemia (ischemic stroke) can be seen in the cerebral capillary compartment within the neurovascular unit. Cerebral capillaries consist of the endothelium, the extracellular matrix (ECM) of the basal lamina, and the astrocyte end-feet which communicate with the neurons they serve. Pericytes and ancillary cells contribute to cerebral vascular structures. Events within the capillary and the microvascular endothelium-matrix-astrocyte complex contribute to injury within the neuropil which lies below the resolution of clinical detection systems

Focal ischemia causes loss of patency within the dependent microvasculature (focal "no-reflow"), restoration of which is possible and can rescue injury extent. The loss of patency coincides with rapid alterations in the relationships within the endothelium-matrix-astrocyte complex. This includes abrupt coincident i) decreases in endothelial cell $\beta 1$ integrin and $\beta 4$ integrin expression, ii) increases in integrin $\alpha v \beta 3$ expression, iii) decreases

in astrocyte αβ-dystroglycan, iv) alterations in matrix composition, and v) changes in permeability that are reproducible in in vitro systems. Changes in cell function accompany these alterations in adhesion, which do not involve cell demise. These structural alterations demonstrate that adhesion receptor changes and alterations in matrix can significantly affect the permeability barrier.

Ischemia can modulate the ultrastructural characteristics of both endothelial cells and astrocytes in regions of neuron injury, as also demonstrated in vitro. These changes have implications for intra- and inter-cellular signaling processes within the microvasculature and within the neurovascular unit.

The impact of innate inflammation within the neuropil on microvessel structure involves the participation of activated microglia, which release (pro-)MMP-9 and cathepsin L, both capable of modulating matrix structure. Containing these processes to the bed of injury is the focus of experimental treatment approaches.

All of these events are initiated by reduction in perfusion to the microvessel beds, which, without intervention, can lead to persistent low perfusion.

CURRICULUM VITAE

ANTON ALVAREZ

SPAIN

Medical Doctor (M.D.), University of Santiago de Compostela (1987)
Diploma of Specialist in Neuroendocrinology, University of Santiago de Compostela (1988)
Graduate in Psychology, University of Santiago de Compostela (1988)
Doctorate in Psychiatry, University of Santiago de Compostela (1988-1990)
Resident Research Fellow of the Ministry of Education and Science (1988-1992)
Department of Psychiatry, Santiago University (1988-1991)
Madrid Complutense University (1992)

Psychiatry Doctor (PhD), Department of Psychiatry, Madrid Complutense University (1997)
Dr. Àlvarez has 22 years experience in Basic and Clinical Research on Alzheimer's disease.
He was involved in more than 150 research projects, including projects funded by Public Institutions, pharmaceutical R&D studies, industrial and R+D+I projects, epidemiological studies and two projects funded by the European Comunity: (1) MimoVax:
Alzheimer's disease treatment targeting truncated AB40/42 by active immunisation (an STREP -Specific Targeted Research Projects- Project approved through the Six Framework Programme of the European Community to develop and test a vaccine for Alzheimer's disease). Period: 2006-2010. (2) BIOMED-PL-950523-European Concerted Action on Pick's Disease. Period: 1995-1998.

As a result of the research activity developed during this period, Dr. Àlvarez published more than 120 scientific articles in national and international journals and books. In addition, Dr. Àlvarez is actively involved in several scientific forums of his specialty (Congresses, Research Groups, Scientific Journals and Associations).

JAROSLAW ARONOWSKI

USA

Dr. Aronowski is Professor and Vice Chair of Neurology, Director of Stroke Research, and the Roy M. and Phyllis Gough Huffington Chair in Neurology at the University of Texas Health Sciences Center (UT-HEALTH). He received his degrees from the Warsaw Medical School and Polish Academy of Sciences. In the past two decades, Dr. Aronowski has served on over 100 NIH and AHA study sections and acted as a Member of the Planning Group to Establish NIH Future Goals/Priorities in Stroke Research - NIH, NINDS. Over the past 25 years, his research has been sponsored continuously by several grants from NIH. Discoveries in his lab have resulted in 3 stroke clinical

trials. He is the Associate Editor for Basic Science for the Stroke journal. His research focuses on understanding the cellular and molecular mechanisms underlying the pathology of acute cerebral ischemia, reperfusion injury, and secondary injury after intracerebral hemorrhage, with emphasis on the role of transcription factors (specifically NF-κB, Nrf2 and PPAR), neuroinflammation (including role of microglia and oligodendroglia), stem cell therapy, and the use of ultrasound in tPA-mediated thrombolysis. He currently serves as a Treasurer Elect and member of the Financial Committee for the International Society for Cerebral Blood Flow and Metabolism.

OVIDIU BAJENARU

ROMANIA

1983	: M.D. at the Faculty of Medecine of University of Medicine and Pharmacy "Carol Davila" Bucharest
1983-1985	: post graduate hospital stagium in University Hospital of Emergency Bucharest
1985- 1989	: resident of neurology
1985	: assistant professor – University of Medicine and Pharmacy "Carol Davila" Bucharest- Department of Neurology of the University Hospital of Emergency Bucharest
1989	: specialist in neurology, confirmed by the Ministery of Health of Romania
1993	: Ph.D. at the University of Medecine and Pharmacy "Carol Davila" Bucharest - senior lecturer of neurology - Head of Department and Medical Chief (University Hospital of Emergency, Bucharest
1994 - 1999	: Associate Professor of Neurology
1999 (since)	: Professor of Neurology at the University of Medicine and Pharmacy " Carol Davila" Bucharest and Chairman of the Neurology Department of the University Hospital of Emergency Bucharest
2006:	: Doctor Honoris Causa - University „Ovidius" – Constanta (Romania)
2011	: Director of Department of Clinical Neurosciences - University of Medicine and Pharmacy " Carol Davila" Bucharest
2013 (since)	: Corresponding member of the Romanian Academy of Medical Sciences

Other professional activities :

2000-2004	: Vice-Dean of the Faculty of Medecine - University of Medecine and Pharmacy " Carol Davila" Bucharest
2001-2013	: President(founder) of the Romanian Society of Neurology
2013(since)	: Honorary President ad vitam of the Romanian Society of Neurology
2003-2009	: member of the Scientific Committee of ECTRIMS
2005-2009	: member of the Executive Committee of the European Society of Neurology
2011 (since)	: member of the National Committee of Habilitation of the Romanian Ministery of Education for PhD accreditation and high academic degrees

Post graduate training :

1992 - 1994 : post graduate training in clinical neurology and functional investigations of the nervous system at University " Rene Descartes"(Paris) : C.H.U. Sainte-Anne (Neurology) and C.H.U. Cochin – Port Royal (Functional Investigations of the Nervous System) and training in neuroendocrinology

1996 : second medical competence (confirmed by the Ministery of Health of Romania) in "Diagnosis in Neurological Diseases by MRI".

1997 : assistant of clinical research in pharmaco-clinical trials (Paris)

2009, 2011 : International training for methodology in clinical research

Fields of interest for the scientific research

- dementia and neurodegenerative diseases (in particular Parkinson's disease)
- multiple sclerosis
- stroke
- experimental and clinical study of sleep disturbances in the neurological and neuroendocrinologic diseases
- more than 450 scientific papers published and reported in different national and international scientific meetings
- ISI Web of Science: h-index : 8
- 5 medical books and monographies (published in Romania)
- co-author (1 chapter) to the "International Neurology - A Clinical Approach" (eds. ROBERT P. LISAK, DANIEL D. TRUONG, WILLIAM CARROLL, ROONGROJ BHIDAYASIRI), Wiley-Blackwell , 2009
- Country Principal Investigator – in more than 20 international, multicentric clinical trials
- Principal Investigator of the research site – in more than 30 international and national multicentic trials
- Member of the Steering Committee of PRECISE trial

Other activities:

- coordinator of the Continuous Medical Education (EMC) national program of the Romanian Society of Neurology for neurologists in Romania
- coordinator and author of the Guidelines for diagnosis and treatment of neurological diseases (agreed by the College of Medecins of Romania) main author of the national guidelines for Parkinson's disease, Multiple Sclerosis and Dementia
- coordinator of the National Program of the National House of Insurance and Ministery of Health, for treatment of patients with neurological diseases (2000 - 2015)
- coordinator of the first medical team in Romania for DBS in Parkinson's disease.
- chief-editor of Romanian Journal of Neurology (the official journal of the Romanian Society of Neurology)

Scientific affiliation :

- Romanian Society of Neurology (Honoray President ad vitam)
- UEMS – European Board of Neurology (Secretary General – elected in 2010)
- European Neurological Society (ENS) – member of the Executive Committee between 2005 – 2009
- European Stroke Organization
- European Federation of Neurological Societies (EFNS) and European Academy of Neurolgy (since 2014)
- American Academy of Neurology (cooresponding member)
- Danube Neurological Association (Vice-Secretary General – elected in 2011)
- ECTRIMS (member of the Scientific Council 2003-2009)
- New York Academy of Sciences
- American Academy for Advancement in Science
- Movement Disorders Society
- Romanian Association for the Study of Pain
- Romanian Society for the Study of Neuroplasticity (founder president of honour)

2005, 2006, 2010, 2011: awarded by the Prize of Excelence in Neurology for the scientific activity in Romania (decided by a National Jury organized by the Health Chamber of the Romanian Parliament)

2008: awarded by the Romanian Society of Internal Medicine for the best scientific activity in a related medical speciality
2014: awarded by the International Brain Foundation and Romanian Academy of Medical Sciences, for excellency in the development of management of patients with multiple sclerosis in Romania
Investigator in an International Program of Research for genetic factors in stroke patients; Country Principal Investigator – in more than 30 international, multicentric clinical trials;
Principal Investigator of the research site – in more than 30 international and national multicentic trials

NATAN BORNSTEIN

ISRAEL

EDUCATION

1970-73	University of Sienna, Medicine, Sienna, Italy
1973-79	Technion Medical School, Hifa, Medicine, MD, 1979

Date of receiving specialixation certificate: 11 September, 1984
Title of Doctoral dissertation: Dextran 40 in acute ischemic stroke
Name of Supervisor: Dr. Jacob Vardi

FURTHER EDUCATION

1978-83	Tel-Aviv University, Sackler Faculty of Medicine, neurology (residence), Israeli Board certified in Neurology, 1983
1979-83	Tel-Aviv University, Sackler Faculty of Medicine, Post graduate studies in Neurology
1984-87	Sunnybrook Medical Center, University of Toronto, M.R.C stroke, Fellowship

ACADEMIC AND PROFESSIONAL EXPERIENCE

1982-1995	Tel-Aviv University, Neurology, instructor
1991-present	European stroke Conference (ESC), Executive committee
1995-1999	Tel-Aviv University, Neurology, Senior lecturer
1995	Eliprodil CVD 715 clinical trial, Steering Committee
1995-1997	International Stroke Study (IST), Steering Committee
1995-1999	American Academy of Neurology, Member of the International Affairs Committee
1996	Asymptomatic Carotid Stenosis and Risk of Stroke(ACSRS), Advisory Committee
1996-present	The Mediterranean Stroke Society (MSS), President
1996-2002	EFNS, Management Committee
1997-2009	Israeli Neurological Association, Secretary
1999-present	Tel-Aviv University, Neurology, Associated Professor
2001- present	European Society Neurosonology and Cerebral Hemodynamics (ESNCH) Executive committee
2005-present	Neurosonolgy Research Group, Executive committee
2006-present	European Master in Stroke Medicine, Member of faculty
2006-2008	NEST II clinical Trial, Steering Committee

2006-present	SENTIS clinical Trial, Steering Committee
2006-present	CASTA Trial, Steering Committee
2006-present	Brainsgate clinical Trial, Steering Committee
2008- present	World Stroke Association (WSO), Vice president
2009-present	Israeli Neurological Association, Chairman
2009-present	European Stroke Organization (ESO), Member on the board of directors
2010-	NEST III clinical Trial, Steering Committee

PROFESSIONAL ACHIEVEMENTS- EDITORIAL BOARD

1991-present	Neurological Research Journal, Guest Editor
1991-present	STROKE, Member of the editorial board
1998-present	European Journal of Neurology, Member of the editorial board
1999-present	Journal of Cerebrovascular disease, Member of the editorial board
2000-present	Journal of Annals of Medical Science, Consulting Editor
2001-present	Journal of Neurological Science (Turkish), Member of the editorial board
2001-present	Acta Clinica Croatica, Member of the editorial Counsil
2003-present	Italian Heart Journal, International Scientific Board
2003-present	Journal of Neurological Sciences, Guest Editor
2004-present	Turkish Journal of Neurology, International Advisory Board
2005-present	Archives of Medical Sciences (AMS) , Member of the Editorial Board
2006-present	Journal of Cardiovascular Medicine, International Scientific Board
2006-present	International Journal of Stroke, Editorial Board
2006-present	Acta Neurologica Scandinavica, Editorial Board
2009-present	American Journal of Neuroprotection& Neurogeneration (AJNN) Member of the Editorial Board
2010	Neurosonology, International Editorial Board
2010	Frontiers in Stroke, Review Editor

PROFESSIONAL ACHIEVEMENTS- REVIEWER

1998-present	Lancet, Ad Hoc reviewer
1998-present	Diabetes and its complications, Ad Hoc reviewer
1999-present	Journal of Neuroimaging, Reviewer
1999-present	Journal of Neurology, Ad Hoc reviewer
2000-present	Neurology, Ad Hoc reviewer
2003-present	Israeli Medical Association Journal (IMAJ), Reviewer
2003-present	Acta Neurologica Scandinavica, Ad Hoc reviewer
2006-present	Journal of Neurology, Neurosurgery & Psychiatry, Reviewer
2010-	European Neurology, Ad Hoc reviewer

MEMBERSHIP IN PROFESSIONAL SOCIETIES

1977-present	Israeli Medical Association
1983-present	The Israeli Neurological Association
1985-present	Stroke Council of the American Heart Association (Fellow)
1986-present	American Academy of Neurology
1986-present	Neurosonology Research Group of the World Federation of Neurology
1987-present	Stroke Research Group of the World Federation of Neurology
1990-2008	International Stroke Society
1995-2008	European Stroke Council
1995-present	Mediterranean Stroke Society (MSS)
1998-present	European Neurosonology Society
2005-present	World Stroke Organization (WSO)
2008-present	Fellow of the European Stroke organization (FESO)

ANTONIO FEDERICO

ITALY

Prof. Antonio Federico, born in Polla (Sa) on the 25.08.48, from 1990 is full professor of Neurology at the University of Siena , Director of the Unit Clinical Neurology and Neurometabolic Disease.

He was Director of the Department of Neurological, Neurosurgical and Behavioural Sciences, University of Siena (2002-2008).

He received the degree in Medicine and specialization in Nervous and Mental Diseases, summa cum laude, at the University of Naples in 1972 and 1975 respectively. He received the Lepetit Award for the best degree dissertation in 1972.
His biological training was in the Institute of Biochemistry as student and after in Physiology of the University of Naples, and in the Centre de Neurochimie of CNRS, in Strasbourg, directed by prof. Mandel where he worked in the years 1973-75. He also collaborated with many international research groups, in different countries where he spent in the past years some times: in Montreal (Prof. Andermann, Karpati and Shoudgbridge), in London (dr A. Harding and prof. Morgan-Hughes), in Toronto (dr.Robinson), in Bonn (prof. von Bergmann) , in Paris (dr.Baumann), in Baltimore (proff. Moser and Naidu), in Oxford (prof. Matthews), etc.
His clinical formation was made at the Medical School of the University of Naples, in the Dept, Neurology, and after in Siena, where he moved on 1980 with his mentor, prof. G.C. Guazzi. Associated professor in Neurology in 1982, since 1990 he is full professor of Neurology, Medical School, University of Siena.
In 2013, he received honoris causa degree in Medicine at University Carol Davila, Bucharest, Rumania.

His present positions are:
- full professor of Neurology, University of Siena, Medical School
- Director of Unit Clinical Neurology and Neurometabolic Diseases, Siena Hospital.
- Director of the Section Neurological Diseases of the Department of Neurological and Behavioural Sciences of the University of Siena since the 2012, at the fusion of this Department in the Dept Medicine, Surgery and Neurosciences.
- Co-Chairman of the Panel of Genetic and Neurometabolic Diseases of the European Academy of Neurology.
- Italian Delegate to the World Federation of Neurology and to European Academy of Neurology Council.
- Past- President of the Italian Society of Neurology (President years 2009-2011)
- From 1995 he is Director of a PhD Programme on Applied Neurological Sciences at University of Siena, from 2004 of the European PhD Programme and European School of Doctorate of Applied Neurological Sciences. Since 2011 he is director of the PhD Programme on Cognitive and Neurological Sciences at University of Siena.
- Director post-graduate School of Neurology, University of Siena
- He is Italian member of the Committee of European Union of Medical Specialists, in the section Neurology.
- Delegate for Research in the Dept. Medicine, Surgery and Neurosciences.
- Coordinator for the Tuscany Region of the Network on Rare Neurological Diseases.
- On 2013, he received Honoris Causa degree from the University Carol Bavila, Bucharest

- Chairman of the Neuromediterraneum Forum
- Editor in Chief of Neurological Sciences, Springer-Verlag Editor.
- On the 2014 was nominate WHO consultant for Rare Neurological Diseases.
- From juin 2014, he is Chairman of the Scientific Committee and Member of the Board of the European Academy of Neurology

In the years 1990-96 he was Secretary of the Italian Society of Neurology. In the years 2006-08 was President of the Italian Society of Neurology.

He coordinated the Study Group on Clinical Neurogenetics of the Italian Society of Neurology.
He has been referee for projects evaluation in the area of Orphan drugs and Orphan diseases for Biomed Projects from EU, for MURST, CNR and Istituto Superiore di Sanità, and other national and international funding agencies, etc.

He is member of the Second Opinion Group of the American Leucodistrophy Association.

Associated editor of Neurological Sciences in the past 3 years. From 2012, Editor-in Chief.

He is author of more than 500 article (more than 300 of them quoted by Pubmed). He is author of a chapter on Cerebrotendinous Xanthomatosis, Vinken and Bruyn Edts, Handbook of Clincal Neurology, vol 49, Neurodystrophies and Neurolipidoses. On the book McKusick's Mendelian Inheritance in Man,. Ed.1992, Catalog of Autosomal Dominant and Recessive Phenotypes he is cited for 3 different diseases. He was editor of the book Late Onset Neurometabolic diseases (A.Federico, K. Suzuki and N.Baumann Edts), Karger 1991, and many other books from Italian and international Publishing Companies.

His main field of interest is related to neurometabolic, neurodegenerative and rare diseases, investigated from a genetic, metabolic, neuroimaging and clinical point of vue.

Summary of the academic involvements:
- Director of the Section Neurological Sciences, Dept Neurological , Neurosurgical and Behavioural Sciences (2000-2012)
- Director of the Research Center for the Diagnosis, Therapy and Prevention of the Neurohandicap and Rare Neurological Diseases, until the 2010
- Vice-Dine of the Medical School, University of Siena (2003-2006)
- Director of the Postgraduate School of Neurology, University of Siena, from 2006 up to date.
- Director of the PhD School in Cognitive and Neurological Sciences, University of Siena (from 2000 up to date)

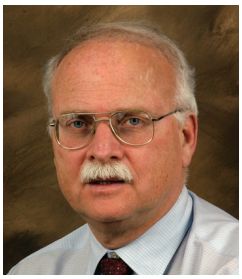
Medical Involvements
- Director of the OU Clinical Neurology and Neurometabolic Diseases, University Hospital of Siena Medical School.
- Director of the Regional Reference Center for Rare Diseases
- Regional Coordinator of the Network for Rare Neurological Diseases, Tuscany Region.
- Member of several Ministery of Health and Regional Committees

National and International Commitments
- President of the Italian Society of Neurology (2009-11)
- Italian delegate to the World Federation of Neurology
- Italian Delegate to the European Union of Medical Specialists (Section Neurology)
- Italian Delegate and Chairman of the Neuromediterraneum Forum and President
- Consultive Member of the European Brain Council
- Editor – in – Chief of Neurological Sciences, Springer Verlag Editor. He is in the Editorial Board of many national and international journals.

- Member of the American Panel United Leucodystrophies.
- Member of the Scientific Committee of AISM (Associazione Italiana Sclerosi Multipla)
- Chairman of the Scientific Committee of the European Academy of Neurology

Member of the Scientific Societies:
- Società Italiana di Neurologia (Secretary, President, Past-President and Member of the Committee)
- Society for the Inborn Errors of Metabolism
- Italian Association of Neuropathology
- SINDEM (Italian Association of Dementias)
- Italian Association for Parkinson's disease
- Italian Association of Neurogeriatrics (Member of the Committee)
- Italian Stroke Forum
- European Academy of Neurology (Co-Chair of the Panel Neurometabolic and Neurogenetic Diseases,

Member of the Board and Chaiman of the Scientific Committee)
- American Academy of Neurology
- World Federation of Neurology
- Neuromediterraneum Forum (President)



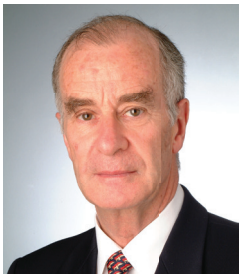
MARC FISHER
USA

Dr. Fisher was affiliated with the University of Massachusetts Medical School for 35 years and is currently an emeritus Professor of Neurology. He began work part-time at Beth Israel Deaconess Medical Center in Boston with an appointment at Harvard Medical School in August, 2014. He has a long track record in performing MRI-based experiments in rat stroke models to evaluate the presence and evolution of the ischemic penumbra. Using diffusion/perfusion MRI his experimental group has evaluated the effects of therapies on the progression of the diffusion/perfusion mismatch. Dr. Fisher has extensive experience in organizing and implementing clinical acute stroke therapy trials with a particular interest in imaging-based trials. He has performed these trials with co-investigators at multiple sites around the world. He has maintained an active clinical practice for many years with an emphasis on patients with cerebrovascular disorders as well as broad range of other neurological illnesses. He has published extensively and has published over 260 peer-reviewed articles with an h-index of 72 and has edited or co-edited 13 books. He currently serves as editor-in-chief of Stroke and will continue in that position until 2020.

FERNANDO GÓNGORA

MEXIC

Fernando Góngora is President of the Iberoamerican Stroke Society (SIECV), and Vice president of the Mexican Stroke Society (AMEVASC). Coordinator of Stroke Program and Director of Stroke Unit at José Eleuterio González University Hospital, Universidad Autónoma de Nuevo León (public University Hospital). Member of Stroke team at Medical Centers in Private Hospitals and Institute of Neurology, ZH Medical Center (private Hospital affiliate to Houston Methodist Medical Center). Specialist of Neurology and Endovascular Therapy by National Institute of Neurology and Neurosurgery at Mexico City, Universidad Nacional Autónoma de México. Master in Neurovascular Diseases at University of Paris VI with Research Fellow in Cerebrovascular Diseases at Bichat Hospital, Paris; complementary endovascular training at Lariboisière and Pitié-Salpêtrière Hospitals in Paris, France. Member of National Research System of CONACYT. He is working for the establishment of the Policy and organizing stroke systems around the country with members of AMEVASC.



WOLF-DIETER HEISS

GERMANY

Wolf-Dieter Heiss, born 31.12.1939 in Zell am See, Austria, graduated in medicine from the University of Vienna, Austria, in 1965. He achieved his training in neurology, neurophysiology, psychiatry and nuclear medicine at the University hospital in Vienna and spent research fellowships at the MIT, Cambridge, USA, the Physiological Institute in Stockholm, Sweden, the Department of Physiology of SUNY, Buffalo, NY and the Department of Neurology of the University of Minnesota, Minneapolis, USA. 1976 he was appointed associate professor at the Department of Neurology of the University of Vienna. In 1978 he became director of the Center for Cerebrovascular Research of the Max Planck Institute for Brain Research and of the Department of Neurology of the City Hospital Cologne-Merheim, Germany. 1981 he was appointed as director at the Max Planck Institute for Neurological Research. 1985 – 2005 he was professor of neurology and chairman of the Department of Neurology of the University of Cologne and director of the Department of General Neurology at the MPI in Cologne. He was president of the International Stroke Society 1992-96, was on the board of directors of the Society for Cerebral Blood Flow and Metabolism, deputy editor of the Journal of Cerebral Blood Flow and Metabolism and at present is associate editor of the Journal of Nuclear Medicine and section editor of Stroke. He was chairman of the program committee of the European Federation of Neurological Societies (EFNS) 1998 - 2001 and was president of the EFNS 2001 – 2005. Since 2005 he is Visiting Professor at the Danube University in Krems, Austria, and since 2009 Adjunct Professor at the McGill University in Montreal, Canada.

His significant portfolio of scientific articles includes 617 papers indexed on Web of Knowledge-ISI, rating a Hirsch index of 63.

In 2013 he became Associated Professor of the Department of Neurosciences, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, Romania.

VOLKER HÖMBERG

GERMANY

MEDICAL DIRECTOR

St. Mauritius Therapy Hospital Meerbusch

PERSONAL DATA

Born 25 July 1954

Married to Priv.-Doz. Dr. Kristina Müller, paediatric neurologist

MEDICAL CAREER

1973 - 1980	School, Universities of Düsseldorf and Freiburg; Elective in Neurology at Boston City Hospital, Boston, Mass.; National Hospital for Nervous Diseases, London
since 1975	Junior researcher in the Department of Neuropsychology at the C. & O. Vogt Institute for Brain Research, Düsseldorf and the Department of Neurology, Freiburg (Prof. R. Jung)
1980 - 1981	Research fellow in the Department of Neuropsychology (Prof. G. Grünewald) at the C. & O. Vogt Institute for Brain Research, Düsseldorf
since 1981	Clinical training in the Department of Neurology (Prof. H.-J. Freund), Heinrich- Heine-University Düsseldorf
since 1985	Senior registrar in the Department of Neurology, Heinrich-Heine-University Düsseldorf
since 1987	Senior investigator for the German Research Council Special Task Force in Neurology at Heinrich-Heine-University (SFB 200 and SFB 194)
1987-2005	Medical director of the Neurological Therapy Center (NTC), Heinrich-Heine-University Düsseldorf
since 1988	Board examiner for Neurology at the local examination board (Ärztekammer Nordrhein)
1989-1997	Vice president of the German Society for Neurological Rehabilitation
1993	Habilitation in Neurology, Heinrich-Heine-University Düsseldorf
since 1995	Board examiner for physical medicine and rehabilitation (Ärztekammer Nordrhein)

1997-2005	Medical director of the Neurological Therapy Center, Cologne
1998-2004	President of the German Society for Neurological Rehabilitation
since 2000	Medical director and head of neurology, St. Mauritius Therapy Hospital, Meerbusch
since 2003	Secretary General World Federation for NeuroRehabilitation (WFNR)
since 10/2004	Vice president of the German Society for Neurological Rehabilitation
since 2005	Panel-Chairman Neurorehabilitation for European Federation Neurological Societies (EFNS)

PETER JENNER

UK

Date of Birth: 6th July 1946

Place of Birth: Gravesend, Kent

Education:

1956-1964	Gravesend Grammar School
1964-1972	Chelsea College, University of London

Degrees and Diplomas:

1964-1967:	B. Pharm(Hons) 2:1, Chelsea College, University of London
1967-1970:	Ph.D., Chelsea College, University of London
1972:	Membership of the Royal Pharmaceutical Society of Great Britain
1987:	D.Sc., University of London
1994:	Fellow of the Royal Pharmaceutical Society of Great Britain
2005:	Fellow of the British Pharmacological Society
2006:	Fellow of King's College London
2008:	Emeritus Professor of Pharmacology, King's College London
2011:	Fellow of the Royal Society of Medicine

Honours and Achievements:

- Elected Fellow of the British Pharmacological Society
- Elected Fellow of King's College London
- ISI Most Cited Author in Neuroscience – Ranked in top 0.5% of all neuroscience authors in the world
- Scientific Impact – Hirsch Index 72 (Admission to National Academy of Sciences USA average 52)
- Winner THES Spinout of the Year 2005 – National Award for the most successful company formed in academia
- Rated in Top Ten Entrepreneurial Academics in the UK – THES/Independent
- National Parkinson's Foundation Centre of Excellence for 'gold standard' research excellence in Parkinson's

disease 2005
- International Movement Disorder Society – Extraordinary Contribution to Movement Disorders (Honorary Membership)

Appointments:

1970-1972	Postdoctoral Fellow in the Department of Pharmacy, Chelsea College, University of London
1972-1978	Lecturer in Biochemistry, University Department of Neurology, Institute of Psychiatry
1978-1985	Senior Lecturer in the above Department
1983-1985	Honorary Senior Lecturer, King's College Hospital Medical School
1985-1989	Reader in Neurochemical Pharmacology, University Department of Neurology, Institute of Psychiatry and King's College Hospital Medical School
1988-2000	Honorary Senior Lecturer, Institute of Neurology
1989-1998	Professor of Pharmacology and Head of Department, King's College London
1993-	Director, Neurodegenerative Diseases Research Centre, King's College London
1998-2004	Head of Division of Pharmacology and Therapeutics, Guy's, King's and St. Thomas' School of Biomedical Sciences, King's College London
2005	Professor of Pharmacology, Guy's, King's and St. Thomas' School of Biomedical Sciences, King's College London
2005-2010	Director of Proximagen Ltd
2008	Emeritus Professor of Pharmacology, King's College London

Editorial Boards:
Journal of Pharmacy and Pharmacology
Polish Journal of Pharmacology
Journal of Neural Transmission (Handling Editor)
Neuropharmacology (Handling Editor 2002 -)
Synapse (European Editor 1990 -)
International Review of Neurobiology (Series Editor)

Past Activities:
Director, Parkinson's Disease Society Experimental Research Laboratories (1988-1999)
Elected Member of Council, Parkinson's Disease Society (1993-1999)
Member of Medical Advisory Panel, Parkinson's Disease Society (1993-1999)
Member of Biochemical Society - Molecular and Cellular Pharmacology Group Committee (until 2000)
President of Watford Branch of Parkinson's Disease Society 2000
Secretary of Basal Ganglia Club
Member of Board of Management, Institute of Epileptology, King's College London
Member of Medical Advisory Board of Bachman-Strauss Foundation, New York 2000-2005
Journal of Neurochemistry (Handling Editor 1998-2008)
Vice-President of European Society for Clinical Pharmacology 2001-2008

Current Activities:
Consultant to the Pharmaceutical Industry

Referee for research grant applications from:
Royal Pharmaceutical Society
Medical Research Council
Wellcome Trust
Parkinson's Disease Society
INSERM, France

ROBERTO MATURANA

CHILE

Dr. Roberto Maturana, graduated from Chile University. During his former studies he was trained at Transcranial Doppler Ultrasound Program, at the Vascular Radiology Department of the Cleveland Clinic foundation USA.

Following his qualifications, he is nowadays Head of the Stroke Unit and Neurology Unit from the Neurology-Neurosurgery Department at Hospital DIPRECA, located in Santiago de Chile, being the first Stroke Unit of the country. At the same hospital, he is also the Head of the Transcranial Doppler Unit.

He was member of the Directory of SONEPSYN (Neurology, Psychiatry and Neurosurgery Chilean Society) and is currently an active member of the Society

Sharing his work at DIPRECA Hospital, he is also the Head of "Los Coihues Neurorehabilitation Clinic", being the responsible for clinic and hospital neuro-rehabilitation patient programs.

DIETER MEIER

AUSTRIA

Dieter H. Meier is the CEO of Neuropore Therapies Inc., a San Diego based company, dedicated to the research and development of drugs interacting with misfolded proteins.

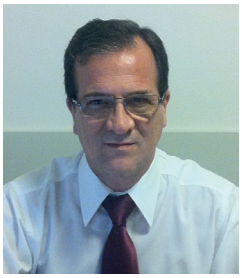
As a board certified neurologist, Dieter H. Meier was engaged over the last 20 years in a number of industry positions, mostly in drug development and general management. His contributions to the drug development at various stages let e.g. to the registration of Pramipexol, Apomorphine and the development of several earlier approaches.

Most recently his team of scientists developed several small molecules interacting with α-Synuclein; one of these molecules was partnered with a large pharmaceutical company and is entering clinical development.

DAFIN F. MURESANU

ROMANIA

Professor of Neurology, Senior Neurologist, Chairman of the Neurosciences Department, Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca, President of the Romanian Society of Neurology, President of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), member of the Academy of Medical Sciences, Romania, secretary of its Cluj Branch. He is also member of 13 scientific international societies (being member of the American Neurological Association (ANA) - Fellow of ANA (FANA) since 2012) and 7 national ones, being part of the executive board of most. Professor Dafin F. Muresanu is a specialist in Leadership and Management of Research and Health Care Systems (specialization in Management and Leadership, Arthur Anderson Institute, Illinois, USA, 1998 and several international courses and training stages in Neurology, research, management and leadership). Professor Dafin F. Muresanu is coordinator in international educational programs of European Master (i.e. European Master in Stroke Medicine, University of Krems), organizer and co-organizer of many educational projects: European and international schools and courses (International School of Neurology, European Stroke Organisation summer School, Danubian Neurological Society Teaching Courses, Seminars - Department of Neurosciences, European Teaching Courses on Neurorehabilitation) and scientific events: congresses, conferences, symposia (International Congresses of the Society for the Study of Neuroprotection and Neuroplasticity (SSNN), International Association of Neurorestoratology (IANR) & Global College for Neuroprotection and Neuroregeneration (GCNN) Conferences, Vascular Dementia Congresses (VaD), World Congresses on Controversies in Neurology (CONy), Danube Society Neurology Congresses, World Academy for Multidisciplinary Neurotraumatolgy (AMN) Congresses, Congresses of European Society for Clinical Neuropharmacology, European Congresses of Neurorehabilitation). His activity includes involvement in many national and international clinical studies and research projects, over 300 scientific participations as "invited speaker" in national and international scientific events, a significant portfolio of scientific articles (120 papers indexed on Web of Science-ISI, H-index: 14) as well as contributions in monographs and books published by prestigious international publishing houses. Prof. Dr. Dafin F. Muresanu has been honoured with: the Academy of Romanian Scientists, "Carol Davila Award for Medical Sciences / 2011", for the contribution to the Neurosurgery book "Tratat de Neurochirurgie" (vol.2), Editura Medicala, Bucuresti, 2011; the Faculty of Medicine, University of Medicine and Pharmacy "Iuliu Hatieganu" Cluj-Napoca "Octavian Fodor Award" for the best scientific activity of the year 2010 and the 2009 Romanian Academy of Medical Sciences "Gheorghe Marinescu Award" for advanced contributions in Neuroprotection and Neuroplasticity.



IGNACIO PREVIGLIANO

ARGENTINA

Dr. Ignacio Previgliano is specialist in Critical Care Medicine and Neurology, Professor of Neurology and Associated Professor of Internal Medicine at Maimonides University School of Medicine. His areas of expertise are Neuro Critical Care, Vascular Neurology and Cognitive Impairment. He has won several awards including one of the 2005 9th Congress of the World Federation of Societies of Intensive and Critical Care Medicine. He has published 57 papers in indexed and non-indexed peer review journal. He is reviewer of neurosurgical and critical care journals, collaborated in several books and has his own textbook "Evidence Based Neuro Critical Care".

JEFFERSON V. PROAÑO

MEXICO

Dr. Jefferson Proaño, graduated from "Unversidad Nacional Autónoma de México". During his studies he was awarded with the "Gabino Barreda" medal for the highest grades of his graduating speciality class. Nowadays he is a neurologist and researcher at "Hospital de Especialidades del Centro Médico Nacional Siglo XXI", located on the heart of Mexico City. He is a member of the Mexican and American Academies of Neurology. At the same time, he is the secretary of the Research Committee of the "Angeles Metropolitano Hospital". He is author of more than twenty articles in indexed journals and he has participated like author or co-author in more than fifteen books.

HARI SHANKER SHARMA

SWEDEN

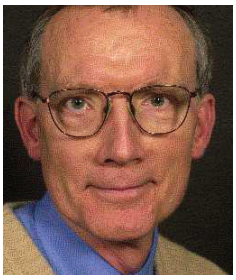
Hari Shanker Sharma, Director of Research (International Experimental Central Nervous System Injury & Repair, IECNSIR), University Hospital, Uppsala University is Professor of Neurobiology (MRC), Docent in Neuroanatomy (UU) and is currently affiliated with Department of Surgical Sciences, Division of Anesthesiology and Intensive Care Medicine, Uppsala University, Sweden. Hari Sharma was born on January 15, 1955 in an Industrialist town Dalmianagar (Bihar), India. He did his Bachelor of Science with Honors from the prestigious L. S. College Muzaffarpur in 1973 and secured 1st position in his batch. He obtained his Master Degree from Bihar University with special expertise in Cell Biology in 1976 and awarded Gold Medal of Bihar University for securing 1st potion in the 1st Class. Hari Sharma joined the group of Professor Prasanta Kumar Dey, a neurophysiologist by training in the Department of Physiology, Institute of Medical; Sciences, Banaras Hindu University, Varanasi in 1977 to obtain Doctor of Philosophy Degree (D.Phil.) in Neurosciences and was awarded Ph.D. in 1982 on "Blood-Brain Barrier in Stress." Hari Sharma after carrying out a series of Government of India funded Research Projects on the BBB and brain dysfunction (1982–1987), joined the lab of Neuropathology at Uppsala University with Professor Yngve Olsson in 1988 to investigate passage of tracer transport across the BBB caused by stress or traumatic insults to the Brain and Spinal cord at light and electron microscopy. Dr. Sharma awarded the prestigious Alexander von Humboldt Foundation Fellowship of German Government (1989–1991) to work on hyperthermia induced BBB dysfunction at the ultrastructural level in the laboratory of Professor Jorge Cervós-Navarro (a living "Legend in Neuropathology in Europe"). Dr. Sharma joined again Uppsala University and established a network of collaboration on "Experimental CNS Injury Research Group" as a lead investigator with eminent collaborators in various parts of Europe, USA, and Australia (1991–). On his work on hyperthermia Dr. Sharma received the prestigious Neuroanatomy award "Rönnows Research prize" of Uppsala University for "best neuroanatomical research of the year 1996" followed by the Award of the Degree of Doctor of Medical Sciences of Uppsala University in Neuroanatomy in 1999 and selected for the Best Thesis Award of the Medical faculty, "The Hwassers Prize" of 1999. On his meticulous works on the Blood Brain barrier and Brain edema (2000–2003) Dr. Sharma earned the prestigious title of "Docent in Neuroanatomy" of Medical Faculty, Uppsala University in April 2004. Currently his main research interest is Neuroprotection and Neuroregeneration, in relation to the Blood-brain barrier in stress, trauma, and drugs of abuse in health and disease.

Dr. Sharma on his research on brain pathology and neuroprotection in different models received the prestigious awards from The Laerdal Foundation of Acute Medicine, Stavanger, Norway, in 2005 followed by Distinguished International Scientists Collaboration Award by National Institute on Drug Abuse (NIDA), Baltimore, MD (2006–2008). His recent work on 5-HT3 receptor mediated neuroprotection in morphine withdrawal induced neurotoxicity won the coveted prize of Best Investigator Award 2008 and Best Scientific Presentation by European Federation of the International Association for Study of Pain (ISAP), and Awarded during their VI Annual Meeting in Lisbon, September 9–12, 2008. His recent research is aimed to find out the role of nanoparticles in Neurodegeneration and Neuroprotection using various treatment strategies that is supported by European Aerospace Research and Development (EOARD), London, UK and US Air Force Research Laboratory, Wright Patterson Air Force Base, Dayton, Oh, USA. On his works on Blood–brain barrier in hypertension and diabetes together with Romanian colleagues, University of Medicine and Pharmacy "Iuliu Hatieganu," Cluj-Napoca, Romania awarded Dr. Sharma with Honorary Doctorate of Medical Sciences in 2009. Dr. Sharma's work over 30 years on the blood-brain barrier and brain edema won him the US Neurosurgeon Dr. Anthony Marmarou Award (2011) by the International Brain Edema Society at their 15th Congress in Tokyo, Japan, November 20–24, 2011. His works on Nanoneuroscience and development of nanomedicine to treat the CNS injuries has

won accolades at various Government and International Scotties or Organization across the World. Accordingly Dr Sharma was decorated with the most prestigious "Hind Rattan Award 2012" (Jewel of India) on the eve of Republic Day of India 25th January 2012 and Mahatma Gandhi Pravasi Gold Medal on October 12, 2012 in House of Lords, London, UK. Based on his outstanding contribution in Nanoneuropharmacology and nanodrug delivery to treat central nervous system (CNS) diseases including Neurodegenerative diseases such as Alzheimer's and Parkinson's Hari Sharma bestowed with Prestigious Gujarat Govt. International Visionary Award 2012 in a glittering function in Ahmedabad, Gujarat on Nov 23, 2012. His further research on co-morbidity factors e.g., hypertension or diabetes may alter pathophysiology of brain injuries and require higher drug dose or nanodrug delivery of neuroprotective agents to minimize brain dysfunction is recognized by Govt. of India by presenting him one of the coveted "Bharat Jyoti Award 2013" (Glory of India) by His Excellency Governor Balmiki Prasad Singh in Hotel Le Meridien, New Delhi on Jan 12, 2013. Dr Sharma also received the highest Award of the Govt. of India "Navrattan Award 2013" (Nine Jewels of India) on the eve of 64th Republic Day of India (25th January 2013) by His Excellency Governor Bhishma Narain Singh, in Ashok Hotel, New Delhi. Hari Sharma is Founding President of the Global College of Neuroprotection & Neuroregeneration (2004-); Elected President of International Association of Neurorestoratology (IANR) (2014-); and selected Senior Expert of Asia-Pacific CEO Association, Worldwide (APCEO) (2012-) for his contribution to uplift scientific research in many countries Globally that may have better economic and social benefit for the mankind. Hari Sharma awarded coveted National Award "Sword of Honor" 2015 by Govt. of India on the eve of 66th Republic Day of India 25th January 2015 in New Delhi Eros Hotel International during the 34th Non-resident Indian (NRI) conclave by Speaker of Lok Sabha (Indian Parliament) the Hon'ble Mrs Meira Kumar of Indian national Congress (INC) Party for the continued extraordinary achievement in nanomedicine for public health awareness and possible therapeutic measures.

Based on his expertise in Nanoneuroscience, Hari Sharma was also invited to organize and chair Nanosymposium in Society for Neuroscience meetings in Chicago (2009), San Diego (2010), Washington DC (2011), New Orleans (2012), San Diego (2013) and Washington DC (2014, Nov 15-19, 2014); Chair Neurobiology Symposium 14th Int. Amino Acid & Peptide, Vienna, Austria; Keynote speaker & Chair Nanotechnology-2015, Frankfurt, Germany. Hari Sharma is also the recipient of Prestigious US TechConnect Global Innovation Award 2013 at the National Innovation Summit & Innovation Showcase, Washington DC May 12-16, 2013 on his work on Nanowired cerebrolysin in Neuropathic Pain. Hari Sharma Served as one of the Poster Judges in 2014 Annual Meeting of American Association fo Advancement of Science (AAAS) Held in Chicago, IL, USA Feb 13-17, 2014. Hari Sharma has published over 400 research papers, 85 reviews, 14 monographs, and 80 international book chapters and edited 18 book volumes. He served as Guest Editor of Curr. Pharm. Desig. (2005, 2007, 2010–); J Neural. Transmiss. (2006, 2011–) and is the founding Editor-in-Chief of Int. J. Neuroprotec. Neuroregen. (2004–), UK and the European Editor of Central Nervous system-Neurological Disorders Drug Target (2013-). Dr. Sharma is on board of various International Journals including CNS and Neurological Disorders-Drug Targets, USA (2010), Journal of Neurodegeneration and Regeneration, USA (2009–); Austin Journal of Nanomedicine & Nanotechnology (2014-); and is associate editor of Journal of Nanoscience and Nanotechnology (Nanoneuroscience 2006–), USA, Review Editor—Frontiers in Neuroengineering (2007–), Frontiers in Neurorestoratology, and Associate Editor of Frontiers in Aging Neuroscience (2008–), Frontiers of Fractal Physiology (2010–), Switzerland, Journal of Neurorestoratology, Dove Medical press, London, UK (2012–), WebMD Central, Neurology Faculty, Advisory Board Member (2010–), World Journal of Pharmacology (2011–), Journal of Physical Medicine and Rehabilitation, USA (2012–). Dr. Sharma served as volume editor of several progress in Brain research series (Volumes 104, 115, 162 and 180), International review of Neurobiology (Volume 82 and 102) and other Springer Volumes on Spinal cord injury (1988) and Handbook of Neurochemistry (2009) apart from stand alone books (Elsevier, Springer and Academic Press since 1994). Dr. Hari Sharma is invited to join several National Academies of repute including New York Academy fo Science, USA (since 1994–); International Academy of Stress, New York (2003–), Swedish Academy of Pharmaceutical Sciences (2010–). Dr. Sharma has served as an expert evaluator and advisor to various Boards, Councils and Institutions for their Research Grants including Wellcome Trust, London, UK (2011–); Catalan Agency for Health Information and Quality, TV3 (2010–), European Commission Projects (2002–), European Nanomed Council (2009–), Ministry of Health Science Foundation; Medical research Council and University Commission of Grants in various countries in Europe, USA, UK, Canada, Hong Kong, Singapore and in Australia. Some of the notable organizations include: Australia and New Zealand Health Council (2000–); University Commission of Grants, Hong Kong (2002–), Singapore Medical Council, Singapore (2003–); UK Charity Organization "Research

on Ageing: Help the Aged" (2003–); Euro Nanomed (2010–). Dr. Sharma is designated as ambassador of the City of Uppsala 2007, by Uppsala County administration and Uppsala Tourism for promoting Uppsala, Sweden as International Research Collaboration/Meetings and Conference Destination. Dr. Hari Sharma is married to Aruna Sharma (nee Bajpai) since 23rd April 1979 and has two sons. His political affiliations belong to Swedish Social Democrat Party (Socialdemokraterna, Sverige) where he is associated with the development of Education and Research matters in Sweden actively.



STEPHEN SKAPER

ITALY

STUDIES: B.S. (chemistry) Illinois Institute of Technology (1969); Ph.D. (biochemistry) University of South Dakota (1973); Laurea in chemistry, University of Padua (1990)

CAREER: NIH Postdoctoral Fellow, Department of Medicine, University of California, San Diego (1973-1976); Fellow in Human Genetics, Department of Pediatrics, Case Western Reserve University, Cleveland, Ohio (1977); Postgraduate Research Biologist, Department of Biology, University of California, San Diego (1978); Assistant Research Biologist, Department of Biology, University of California, San Diego (1979-1982); Associate Research Biologist, Department of Biology, University of California, San Diego (1983-1987); Head, Laboratory of Neuropharmacology, Neuroscience Research Laboratories, Fidia S.p.A. - Abano Terme, Italy (1987-1993); Principal Scientist and Head, Laboratory of Cell Biology, Researchlife S.c.p.A. (a Lifegroup Company), Biomedical Research Center, St. Thomas Hospital, Castelfranco Veneto (TV), Italy (1993-1996); Visiting Professor, Department of Pharmacology, University of Padova, Padova, Italy (1997); Assistant Director, Molecular Neurobiology Research, SmithKline Beecham Pharmaceuticals, New Frontiers Science Park, Harlow, United Kingdom (1998-2001); Senior Team Leader, Migraine and Stroke Research, Neurology & GI Centre of Excellence for Drug Discovery, GlaxoSmithKline R & D Limited, Harlow, United Kingdom (2002-2003); Senior Team Leader, Neuro Cell Sciences/ Neurodegeneration Research, Neurology & GI Centre of Excellence for Drug Discovery, GlaxoSmithKline R & D Limited, Harlow, United Kingdom (2004-2007); Senior Team Leader, Target Validation Dept (Cognition and Pain), Centre of Excellence for Drug Discovery, GlaxoSmithKline R&D Limited, Harlow, United Kingdom (2008); Adjunct Professor, Department of Pharmacology and Anesthesiology, University of Padua, Faculty of Medicine, Padua, Italy (2009-present).

PROFESSIONAL MEMBERSHIPS: Sigma I (The Scientific Research Society); Phi Lambda Upsilon (honorary chemistry society); Alpha Chi Sigma (professional society in chemistry/chemical engineering); Society for Neuroscience; International Society for Cerebral Blood Flow and Metabolism

JOURNALS EDITED: Editor-in-Chief, CNS & Neurological Disorders – Drug Targets; Associate Editor, American Journal of Neuroprotection and Neuroregeneration; Editorial Board Member, Nature Scientific Reports (Neuroscience); Councilor, International Association of Neurorestoratology

REVIEW PANELS: The Wellcome Trust (UK), Biotechnology and Biological Sciences Research Council (BBSRC) (UK), Austrian Science Fund (ad hoc review panel to evaluate interdisciplinary doctoral programmes in neuroscience)

RESEARCH INTERESTS: Molecular biology and cellular mechanisms of cell death in CNS aging, neurodegenerative

disorders and neuroinflammation, astrocyte-microglia interactions, oligodendrocyte biology and diseases of demyelination. Track record of drug discovery project leadership in kinases, ion channels, G-protein-coupled receptors, DNA repair enzymes, growth factors, identification and optimization of tools for target validation studies, utilising RNAi, conditional and viral knockdown\outs\ins, transcriptomics, proteomics and in vitro cell-based disease or mechanism relevant assays in rodent systems.

PUBLICATIONS: OVER 290 publications in the neurosciences, including book chapters and symposia proceedings.

PATENTS: Pharmaceutical compositions containing monosialoganglioside GM1 or derivative thereof suitable for the treatment of Parkinson's disease (Patent No.: US 6,620,792 B1), use of CRF receptor agonists for the treatment or prophylaxis of diseases, for example neurodegenerative diseases (US 2003/0186867 A1), treatment of conditions with a need of GSK-3 inhibition (PCT WO 02/062387 A1), use of CRF receptor agonists for the treatment or prophylaxis of diseases, for example neurodegenerative diseases (PCT WO 01/72326 A1), use of monosialoganglioside GM1 or N-dichloro-acetyl-lyso-GM1 for preventing or reversing neuronal degeneration induced by long term treatment with L-DOPA in the therapy of Parkinson's disease (EP 0 770 389 A1)

REVIEWER FOR JOURNALS: Journal of Neuroscience, PNAS, Nature Reviews, The FASEB Journal, Journal of Neuroinflammation, Neurobiology of Disease, Neurobiology of Aging, Glia, Neuroscience, Apoptosis, PLoS One Biology, Journal of Pharmacology and Experimental Therapeutics, British Journal of Pharmacology, Neuropharmacology, European Journal of Pharmacology, Journal of Neurological Sciences

ROBERTO VENTURA

URUGUAY

Dr. Roberto Ventura, original from Uruguay; graduated as doctor in 1984 from "Facultad de Medicina de la República Oriental de Uruguay". After that, he continued his studies at "Instituto de Neurología de la Facultad de Medicina de la República Oriental del Uruguay"; obtaining his neurologist degree in 1988. Four years later he also achieved the psychiatrist degree. Nowadays, his main activity is developed as Head of Neurology at the Spanish Association. Parallel, he also is Neuropsychology Assistant Professor at Neurology Institute. His qualifications as psychiatrist are well known in the Neuropsychiatry Uruguayan Society, where he is currently the president.

GREGORY DEL ZOPPO

USA

Dr. del Zoppo has contributed to the science of acute treatment strategies for ischemic stroke and of the impact of ischemia on the cerebral microvasculature. He was a pioneer of the acute clinical use of plasminogen activators for the treatment of thrombotic/thromboembolic stroke in the early 1980s. In consequence his group has focused on microvessel/neuron responses in the acute evolution of post-ischemic cerebral injury in experimental systems including non-human primate models to murine in vitro systems, and in clinical trial design. Contributions of the experimental work on cerebral microvessel responses in focal ischemia (ischemic stroke) include the focal "no-reflow" phenomenon, the role of peripheral inflammatory responses to microvessel events, acute alterations in microvessel structure, acute endothelial- and astrocyte-matrix adhesion receptor and matrix alterations in edema and hemorrhagic transformation, and related glial events associated with neuron injury. Current attention is on the relationships and interactions among endothelial cell and astrocyte adhesion to the matrix, the tight junction and adherens complexes, and their management of the permeability barrier under nromoxia and injury. Those studies support the concept of the "neurovascular unit." Dr. del Zoppo has also designed and conducted clinical trials in acute interventions in ischemic stroke, and problems of hemostasis and thrombosis. Currently, he serves on both DSMBs and Advisory Boards for clinical trials in ischemic stroke.

Following research work at the California Institute of Technology, Dr. del Zoppo trained in internal medicine and hematology, and at the Institute of Neurology, Queen Square (London). Experimental and clinical programs were undertaken at The Scripps Research Institute, the Klinikum RWTH Aachen (Gastprofessur der DFG), and the University of Washington. For this work Dr. del Zoppo received the Javits Neuroscience Investigator Award, election to the AAP, the ANA, and the Japanese Society of Neurology, and the 2012 Willis Lecture Award of the AHA/ASA. He is currently Professor of Medicine (in the Division of Hematology) and Adjunct Professor of Neurology at the University of Washington.

CONGRESS VENUE

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REGISTRATION DESK

All materials and documentation will be available at the registration desk located at SSNN booth.
The staff will be pleased to help you with all enquiries regarding registration, materials and program. Please do not hesitate to contact the staff members if there is something they can do to make your stay more enjoyable.

GENERAL INFORMATION

LANGUAGE

The official language is English. Simultaneous translation will not be provided.

CHANGES IN PROGRAM

The organizers cannot assume liability for any changes in the program due to external or unforeseen circumstances.

NAME BADGES

Participants are kindly requested to wear their name badge at all times. The badge enables admission to the scientific sessions and dinners.

FINAL PROGRAM & ABSTRACT BOOK

The participants documents include the program and abstract book which will be handed out at the registration counter.

COFFEE BREAKS

Coffee, tea and mineral water are served during morning coffee breaks and are free of charge to all registered participants.

MOBILE PHONES

Participants are kindly requested to keep their mobile phones turned off while attending the scientific sessions in the meeting rooms.

CURRENCY

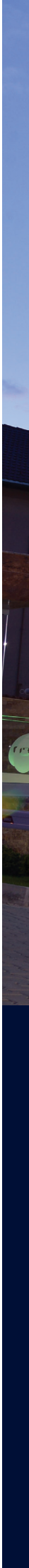
The official Mexican currency is Mexican Peso (MXN).

ELECTRICITY

Electrical power is 120 volts, 60 Hz. Plug Type A (USA) are standard.

TIME

The time in Mexico is Eastern Standard Time (GMT-5).



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